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formulating a composition comprising both an irritant and an anti-irritant simultaneously, and Williamson teaches the use of NO synthase inhibitors for treatment of "various chronic and acute inflammatory conditions." Thus, according to the Office Action, one of ordinary skill in the art would have been motivated to substitute Williamson's NO synthase inhibitor as an anti-irritant in Hahn's composition. Applicant respectfully traverses this rejection.

In order to render an invention obvious, the references cited must suggest the desirability of making the proposed substitution or combination. See M.P.E.P. § 2143.01; *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) (when a rejection depends on a combination of references, there must be a showing that there is a teaching, suggestion, or motivation in the references to make the substitution or combination, not merely that it could have been made); *In re Dembiczak*, No. 98-1498 (Fed. Cir. April 28, 1999) (*prima facie* obviousness not established unless a showing of a teaching, suggestion, or motivation to make the substitution or combination is made). Neither of the references cited by the Examiner teach or suggest the use of NO synthase inhibitors as anti-irritants, as claimed by Applicant. Thus, one of ordinary skill in the art would not have been motivated by either reference to combine the references or make the claimed substitution in order to achieve the desired result. As there has been no showing that the references suggest the substitution or combination, *prima facie* obviousness has not been established.

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Hahn teaches the use of formulations containing a divalent strontium cation to suppress skin irritation, particularly due to topical application of products containing other irritating ingredients. See column 9, line 59 to column 10, line 10. However, as admitted at page 2 of the Office Action, Hahn does not disclose the use of NO synthase inhibitors as anti-irritants. Williamson does not remedy this deficiency of Hahn.

Williamson teaches the use of NO synthase inhibitors for the treatment of acute or chronic inflammatory disease. See column 2, lines 47-41. Inflammation and irritation are clearly distinct reactive symptoms, with corresponding distinct sensations and treatments. Neither reference suggests that an anti-irritant would work to relieve inflammation, or vice versa, or that one of ordinary skill in the art would treat inflammation with an anti-irritant, or vice versa. Thus, there is no motivation in either reference to use an anti-inflammatory agent as an anti-irritant, and likewise, no motivation to combine these references.

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## Conclusion

In view of the foregoing remarks, Applicant respectfully requests the reconsideration and reexamination of the pending claims, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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